INFO SHEET
Veterinary Services

United States Department of Agriculture
Animal and Plant Health Inspection Service
October 1996

Antimicrobial Susceptibility Testing: Frequently Asked Questions

The following list of questions and answers were developed jointly by the Antimicrobial Susceptibility Monitoring Working Group. The group is composed of individuals from FDA, CDC, and USDA (APHIS and ARS). We hope that this information will help to clarify the reasons for initiating the monitoring system, how the monitoring system will operate, and how the information will be used.

1. Why look at antimicrobial susceptibility at all? Is it really that big of a problem?

Many groups such as the Institute of Medicine and the American Society of Microbiology have identified the emergence of antimicrobial resistant strains as a worldwide issue of critical importance. So far much of this concern has focused on human pathogens; however, there is growing interest in animal pathogens to determine whether the same types of resistance patterns exist.

2. Why are we looking at Salmonella instead of some other animal pathogen?

Salmonella spp. represent a starting point for monitoring susceptibility patterns of animal pathogens. Salmonella spp. are also commonly isolated from animals and have been associated with foodborne disease. The reason to start with Salmonella spp. is that a system already exists to aggregate these isolates from a variety of sources. Much of the serotyping of Salmonella isolates of animal origin is done at the National Veterinary Services Laboratories (APHIS) in Ames, IA. Because of this, a large number of isolates representing different serotypes from a wide geographic area are available for testing. The actual testing of the isolates will be done at the National Animal Disease Center (ARS) in Ames, IA, further facilitating the coordination of isolates.

3. Why are we coordinating with CDC and FDA?

As part of the approval process of Ciprofloxacin™, a new fluoroquinolone antimicrobial, the FDA was strongly encouraged to set up a monitoring system to look at susceptibility of various bacteria to a wide range of antimicrobics. The sponsoring company has been required to initiate monitoring for susceptibility in the target organism (in this case E. coli). Further, the Centers for Disease Control and Prevention was initiating a monitoring program for susceptibility of Salmonella isolates of human origin to several antimicrobics in addition to Ciprofloxacin™. CDC also thought it would be important to test Salmonella isolates of animal origin. There was concern that, in order to bring a balanced perspective to interpretation of changing susceptibility patterns, the USDA, because of its long term relationship with the animal industries, access to isolates, and understanding of epidemiology was a prime candidate to coordinate and interpret the data collected on animal isolates.

4. Why are we including human antimicrobials in the susceptibility monitoring?

Producers and veterinarians have been indicating a need for an expanded antimicrobial armamentarium

for years. The susceptibility testing of antimicrobials currently only approved for use in humans is one way to evaluate the potential efficacy of future products for the veterinary market. Given that extra-label use of antimicrobics may occur in food animals, testing many antimicrobics will give a more complete picture of the sensitivity or resistance associated with each particular antimicrobic.

5. Are we looking for a link between animal and human isolate susceptibility?

No. This system is merely descriptive, meaning that all the current system can do is to describe what is happening relative to antimicrobial susceptibility for one particular organism. Emerging resistance to many antimicrobials has been observed among both human and animal pathogens. Some have postulated a link between the emergence of resistant organisms in animal populations and the emergence of resistant organisms in human populations. This system will not answer that question. This system will provide additional information that may serve as a basis for generation of a hypothesis that may be tested using other studies specifically designed to answer the question at hand.

6. What will be done when decreased susceptibility (increased resistance) is demonstrated?

Some of the Salmonella isolates will be resistant to some of the antimicrobials included in the testing. If the resistance is widespread and to a number of antimicrobials, it may prompt the FDA to initiate an education campaign for veterinarians, producers, and other animal health product providers. FDA has stated that education will be the primary approach used when resistance is identified. If resistance is demonstrated to Ciprofloxacin™, it is likely that the FDA will mount a major education campaign in order to stem further resistance development. Prior to any regulatory activity (e.g., label changes or restricted distribution) the findings of resistance will have to be re-confirmed and additional studies conducted.

7. Who will have access to the data from this monitoring program?

The veterinary data will be maintained in a separate system from the human data and will reside at the National Animal Disease Center in Ames, IA. APHIS and ARS will analyze and interpret the data from the veterinary and plant isolates with the help of industry. Summary information will be made available to FDA, CDC, and other interested parties.

8. What about resistance development to illegal drugs among veterinary isolates?

None of the antimicrobials being tested are actually illegal to use; each is approved for some species and indication. Use in a manner other than the labeled use ("off-label" or "extra-label" use) of veterinary drugs approved in the United States is legal as long as certain conditions are met. However, misuse or overuse of antimicrobials does lead to the development of resistance over time. This is why monitoring systems are put into place to track changes over time. Emergence of resistance to off-label use of antimicrobials will be handled in the same way as for approved antimicrobials (i.e., education followed by further monitoring).

9. Will there be trace backs to the farm of origin for "interesting" isolates?

No. The system is not set up for trace backs. Limited information will be available for each isolate tested and what information is available will be kept confidential. There is currently no interest in being able to trace these isolates back to their origin. Again, the purpose of this system is to describe antimicrobial resistance among Salmonella isolates of plant, human, and other animal origin.

10. What is the source of the animal and plant samples?

Samples for the monitoring system will come from a variety of sources including;

- FDA collected vegetable isolates
- NVSL serotyping of animal pathogens

- FSIS carcass and product testing for Salmonella isolates from national studies in the National Animal Health Monitoring System as available
- field isolates from studies conducted by ARS

11. What is the length of this project?

The current project has no estimated sunset. If the surveillance system proves useful it is planned to be continued indefinitely and perhaps expanded to include other organisms.

12. When will the results be reported and by whom?

The results will be reported at least annually. APHIS and ARS will report on the animal and plant isolates and CDC will report on the human isolates. Currently there are no plans to link the release of the results for human, animal, or plant origin isolates. In all cases the plan is to subject information that will be released to a peer review process.

13. Where will the results be reported?

Results will be reported in peer reviewed scientific journals, fact sheets, at scientific and producer meetings, and as news briefings or press releases.

14. Will there be separate reports depending on the source of the isolates (e.g., FSIS, clinical isolates, normal isolates, APHIS)?

The information will be reported without defining an agency. It will be necessary to do some analysis regarding clinical v. normal isolates and the species (i.e., cattle, swine, dog, cat, etc.). Only the minimum amount of information regarding the identification of the isolates will be used and again confidentiality will be maintained.

15. How is funding being provided for this study?

The FDA is providing funds to ARS and CDC for the testing of the isolates. Each of the participating agencies is making the isolates available at no cost. ARS and CDC are also providing some additional funding in the way of personnel costs and facilities.

16. Which antimicrobials are included?

Currently, the following antimicrobials are being tested; Tetracycline, Gentamicin, Amikacin, Apramycin, Ceftiofur, Ciprofloxacin, Trimethoprim/Sulfa, Naladixic Acid, Chloramphenicol, Streptomycin, Sulfamethoxazole, Ampicillin, Ticarcillin, Amoxicillin/Clavulonic Acid, Cephalothin, Kanamycin, and Ceftriaxone. The panel of antimicrobials tested will change periodically as needed. The panel of antimicrobials represent a compromise between those of interest for human and veterinary medicine.

17. What types of conclusions can be drawn from this study?

This study can identify whether there is an emergence, increase, or change in resistance to any one antimicrobial. All other conclusions will be speculative (i.e., regarding why or how the emergence occurred) until additional studies could be conducted.

18. What are the limitations of this study?

This is a descriptive study and analysis of any one isolate does not mean that we can imply any relationship to isolates from other sources. Other types of studies, with specific methods for trace backs would need to be in place to answer relationship type questions.

19. Are the antimicrobial results being provided to the producer from which the isolates originated?

No. The origin of the isolate, as in the specific farm source, is not collected with the isolates. This would preclude any ability to return results to individual producers who owned the animals that were the source of the isolates. State of origin identifiers will be maintained in order to be able to evaluate regional trends and target any educational activities should they be required.

20. How will this information compare to diagnostic laboratory summaries on antimicrobial susceptibilities?

Some diagnostic laboratories collect similar information with a few key differences. In most cases diagnostic laboratory isolates are from clinically ill animals. These animals, and their isolates, probably do not reflect the general population of isolates. Clinically ill animals are more likely to have been treated with antimicrobials. In general, the isolates are likely to have been submitted because they are refractory to common treatments. In addition, the diagnostic laboratories do not aggregate data to a level higher than their service area and there is a lack of standardization among laboratories in how they do antimicrobial susceptibility testing and how they define susceptibility. Differences also exist in the kinds of antimicrobials used. Our testing primarily targets healthy animals. Because of this, it is likely that we will see little resistance. However, if resistance is detected and confirmed, the nature of the origin of the samples will allow us to generate specific hypotheses that may be tested in more focused studies.

In summary: antimicrobial susceptibility monitoring is an issue that will be addressed. The USDA, by playing an active role in the process, brings a balanced perspective to the interpretation of the data and understands first hand the animal industry concerns. The industry, by participating in the program, shows a proactive stance to a worldwide concern. Further the industry may benefit from the demonstration of a lack of sufficient effective antimicrobials. Finally, decision making in the future will be made based on scientific information rather than simply the perceptions of those in a policy making capacity.

If you would like further information on this monitoring system you can contact any of the following people:

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